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T H E S I S

for the Degree of M.D. Edinburgh University.

on

SCOPOLAMINE-MORPHINE NARCOSIS IN LABOUR.

with 126 cases

by

HENRY RUTHVEN LAWRENCE, M.B., Ch.B.

APRIL 1910.

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C O N T E N T S.

TABLE/

P R E F A C E

I am indebted to Professor Sir Halliday Croom and to Dr. F.W.N. Haultain for the opportunity of making these observations while I was House Surgeon at the Royal Maternity and Simpson Memorial Hospital during 1908-9, and for suggestions as to lines of enquiry. I am also under an obligation to Dr. Haultain for assistance in enabling me to consult the literature upon this subject.

I N T R O D U C T I O N.

The function of the medical profession is to alleviate pain and cure disease, these two as a rule going hand in hand. There are some pains, however, which may be regarded as more or less physiological, as they normally exist without the presence of disease, and of these the chief, without doubt, are the pains of labour.

There do exist some persons, of both sexes too, who regard labour pains in all cases as "natural" and as such to be left severely alone so that Nature may take her course without interference. But after consideration of a few points in connexion with this subject most people will admit that in a large number of cases the pains of labour are excessive and should if possible be alleviated.

Many cases of painless labour have been recorded and it seems unreasonable to think that, if such can occur physiologically, the same boon should not if possible, by the aid of science be extended to those women who suffer so very greatly in carrying out their natural function in life.

The, to a large extent, artificial life lived by women in these days of modern civilisation unfits them/

them for the tremendous strain of childbirth; both physically, for their bodies are not nearly so well developed as those of their more primitive and natural living sisters in other parts of the world, and mentally, as (possibly owing to the rapid rate at which we live and the condition of what might be called nervous tension thereby induced) the fear and horror evinced by so many of them for childbirth too plainly shows. This is most often observed in private practice anong the upper classes where labour is often followed by a condition of nervous exhaustion which it is impossible to consider as natural.

Another point of great interest is raised by this observation, for may not the universally declining birthrates of civilised countries be partly due to this fear of the great sacrifice which women must pay to obtain what should be their heart's desire? What then can be done to alleviate the pains of labour? One immediately thinks of the whole range of anaesthetics, general and otherwise. But none of those administered by inhalation such as chloroform, ether, ethyl chloride and so on, can be administered continuously for so long a time, and to such a degree, as is necessary to produce anaesthesia, without the probability of producing serious effects upon the mother, if/

if not upon the child. In addition, the risk of checking the uterine contractions and thus lengthening the labour and introducing elements of danger is great. Of those narcotics and hypnotics whose effects are obtained by internal or hypodermic administration, chloral, morphia and veronal have been tried, among others, but all of these need to be given in toxic doses to obtain a really sufficiently anaesthetic action.

There remains one substance, which has come into use during the last ten years, and which seems to answer to most, if not all, the requirements of an obstetric anaesthetic - and that substance is Scopolamine.-

P H A R M A C O L O G Y.

Scopolamine is an alkaloid of the Atropine series which includes atropine, hyoscyamine, atroscine, scopolamine or hyoscine and some others. Scopolamine is found in the following plants of the order of Solanaceae: Hyoscyamus Niger, Datura Stramonium, Atropa Belladonna, Duboisia Myoporoides, Scopola atropoides according to Cushny (1) and Datura Alba and Scopola Carniolica according to Spencer Sheill (2). The British Pharmacopeia (3) gives the source as Hyoscyamus Leaves and different species of Scopola. There appears to be some confusion as to the names Hyoscine and Scopolamine, owing to the fact that alkaloids bearing these two names, and derived from Hyoscyamus and Scopola respectively, were placed on the market commercially as different drugs. Neither of these was at first a pure alkaloid but further investigation showed that when isolated they were chemically identical. Sheill (2) quotes Martindale and Binz to this effect, the latter giving the formula for the alkaloid as $C_{17}H_{21}N_{04}$. Hare (4) also affirms this and gives the source of the drug as Scopola Atropoides. The essential identity of Hyoscine and Scopolamine is recognised by the United States Pharmacopeia and by the British/

British Pharmacopeia (3) the latter giving the Hydrobromide as the official preparation with a dose of 1/200 to 1/100 gr. and the formula $C_{17}H_{21}NO_4$, HBr, $3H_2O$

It takes the form of "colourless, transparent, rhombic crystals, permanent in the air; odourless; taste acrid, slightly bitter - Solubility - 1 in 1 of cold water; 1 in 13 of alcohol 90%; very slightly soluble in ether or chloroform. Aqueous solution slightly reddens litmus . Aqueous solution precipitated by solution of mercuric chloride, solution of iodine, and also by solution of potassium hydroxide, but not by solution of ammonia or solution of potassium bichromate. It forms with auric chloride a crystalline salt having a melting point of 388·4°F". (Mitchell Bruce.5). I have been in correspondence with Messrs.Burroughs and Wellcome, whose "Tabloid" Hyoscine Hydrobromide (Hypodermic) has been used in all the observations in this series of cases, and in a personal communication from their laboratories I have obtained the following additional information which embodies the latest results of research in this subject.

"Subsequent research has shown that the alkaloid which may be called either Hyoscine or Scopolamine exists in three stereo-isomeric forms, namely, the dextro, laevo and racemic modifications. It has been/

been stated that the laevo form acts twice as strongly as the racemic form on peripheral nerve endings and it also seems probable that some writers use Scopolamine to denote the laevo and Hyoscine to denote the racemic form. This would explain the statement that Scopolamine is more active than Hyoscine. The laevo form exists in the plants, but is liable to be converted wholly or partly into the inactive form during the process of manufacture, and this explains the variation in melting point, optical rotation, and physiological activity of different specimens of Scopolamine Hydrobromide. The laevo base (Scopolamine) bears the same relationship to the racemic base (Hyoscine) as Hyoscyamine to Atropine. Hyoscine Hydrobromide "Wellcome" Brand is laevo-rotatory and this is the drug used in the preparation of "Tabloid" Hypodermic Hyoscine Hydrobromide".

The physiological action of Hyoscine or Scopolamine is something like that of Atropine. Scopolamine however has a depressant action on the central nervous system and a stronger action on peripheral nerve endings. Hare (4) says it causes sleep, sometimes delirium. The circulation is little affected. He gives as the physiological antidote Pilocarpine in full doses if the heart is sound. Cushny (1) gives a somewhat/

somewhat fuller account. He says that the drug depresses the central nervous system causing a feeling of fatigue and drowsiness followed by sleep, which is very natural in character, though its hypnotic effect is less reliable than that of morphia. The circulatory and respiratory centres are not stimulated as in atropine hence blood pressure falls and respiration slows: this latter point being noted also by Lanphear (6), and Jamieson (7), who experimented upon cats The latter found that cats recovered from an overdose of Scopolamine if stimulated with Strychnine and treated by artificial respiration. He therefore suggests this as the logical clinical treatment for Scopolamine poisoning. Cushny points out that the effect on the circulation and respiration is not found clinically in man because the dose is insufficient. Further, he says that sometimes a short stage of excitement precedes sleep, the symptoms being giddiness, uncertain movements, and difficult and indistinct speech. Sometimes symptoms resembling those following atropine may occur such as excitement, restlessness, garrulity and even delirium especially after large doses. The sleep produced lasts 5 to 8 hours and the patient remains somnolent for several hours longer. In one or two cases collapse has been observed. The effects

of/

of paralysis of peripheral nerve endings are mydriasis and loss of accommodation, dryness of the mouth and throat causing thirst, in some cases so intense as to prevent deglutition. Sometimes flushing of the skin of the head and neck, as in the case of atropine, is observed. Cushny (1) concludes by noting that Scopolamine is not so dangerous a drug as others of the series. There seems to be a danger of personal idiosyncracy in individual cases to the action of the drug for, besides differences of minor degree in the reaction to its administration in different persons noted by all who have had any opportunity of using it, at least one case of severe symptoms following its use in minute quantities as a local mydriatic has been reported by Moore (8). Halpenny and Vrooman (9) in a comprehensive paper on this subject point out that the contradictory results obtained by Stella (10) Kochmann (11) Webster (12) and others who have investigated the pharmacdogical action of this alkaloid are probably due to the idiosyncracy of the animals used. It has been shown that dogs can stand very much larger doses of the drug than can man. Perhaps one might also suggest that there may have been differences in the purity and strength of the alkaloids employed. The effects on the circulatory and respiratory centres observed/

observed by Cushny (1) Lanphear (6) and Jamieson (7) were all the result of distinctly toxic doses: in non-toxic doses the circulatory and respiratory centres are slightly stimulated. This is brought out by the remark of Leedham-Green (13) to the effect that Scopolamine and Morphine are given together to obtain the maximum of their hypnotic effect and the neutralisation of their toxic action. That this stimulating action however cannot be very great is shown by the experiments of Nicholson (14) of St.Louis who is quoted by Halpenny and Vrooman (9). He found that he got better narcosis with Scopolamine and Morphine combined than with a larger dose of Morphine alone or combined with Atropine. He also found that repeated daily injections of Scopolamine and Morphine produced no degenerative changes in the heart, liver, or kidneys. The toxic dose of Morphine and Scopolamine together corresponds very closely to that of Morphine alone, and the findings at the post mortem in death from poisoning with the two drugs combined are the same as in poisoning with Morphine alone.

The action of Morphine is so well known that it need not be entered into in detail, suffice it to mention that it causes sleep, having a strong narcotic effect, and at the same time depresses the circulatory and/

and respiratory centres, more especially the latter, so much so, that death in cases of poisoning with morphine is due to respiratory failure. In connection withits use in obstetrics it may be noted that it abolishes the pain of uterine contractions and sends the patient to sleep, but at the cost of also abolishing these contractions themselves and thus leaving the process of labour in statu quo.

The sleep induced by Scopolamine is extremely natural, the patient can be waked up and answers questions sensibly but falls asleep again as soon as he is left alone. A condition of forgetfulness is engendered called amnesia, and on waking up afterwards he remembers nothing of the questions asked him when wakened during his sleep.

The administration of chloroform or ether after injection of Scopolamine and Morphine is not contraindicated in any way, these two drugs having been used by countless surgeons now as precursors to general inhalation anaesthesia. It has been observed by all who have had the opportunity that far less of the latter is required than for cases which have not had Scopolamine and Morphine.

REVIEW of PUBLICATIONS on SCOPOLAMINE-MORPHINE NARCOSIS in LABOUR.

Ten years ago the first report on the use of Scopolamine and Morphine as an anaesthetic was published by Schneiderlin (15) who had a series of 100 cases of operation. Shortly after this further cases were reported by Korff (16) and Blos (17). The dosage they employed was somewhat heroic, namely, 1/6th gr. Morphine and 1/100 th gr. Scopolamine 4 hours before operation, repeated after 2 hours, and again ½ hour before operation. In some cases the total dose reached 1 gr. Morphine and 1/6th gr. Scopolamine. They had a few fatal cases. Since these observations an enormous number of reports have been published of cases operated upon under the influence of these drugs, employed either alone or as a precursor to general inhalation anaesthesia.

In the domain of Obstetrics Steinbuchel (18) was the pioneer of Scopolamine-Morphine Narcosis. In 1902 he published his report of 100 cases. In the years that have followed the method has been used and reported upon by a great many observers. Notable amongst/

amongst these are Gauss' series of 1000 cases, and Kronig's of 1700 cases. Others who have published cases are Preller (19) 220 cases, Steffen (20) 300 cases, Leopold (21) 200 cases, and Bass(22) 107 cases, but this by no means exhausts the list. Some who have had experience of this method condemn it as unsatisfactory, if not actually dangerous, but the majority regard it favourably. The best accounts are undoubtedly those of Kronig (23) (25) and Gauss (24) (25),who had experience of 1700 & 1000 cases respectively, at Freiburg. In his paper Kronig (23) says that Scopolamine plus Morphine produces a peculiar mental condition of amnesia and analgesia which he calls "Dämmerschlaf" - a sleep verging upon consciousness - or"twilight - sleep". This is the condition which it should be the aim of the accoucheur to produce. He uses two solutions, a three hundredth per cent solution of Scopolamine and a one per cent solution of Morphine, so that the dose of either can be regulated without affecting that of the other. The first injection is given when the pains are strong and regular, lasting about 30 seconds with 4 - 5 minutes intervals. The initial/

initial dose is 4½ decimilligrams (0·00045 gram) of Scopolamine and 1 centigram (0·01 gram) of Morphine. The effect is observed from ½ to ¾ hour afterward. The patient sleeps between the pains and wakes and cries out during the pains. Consciousness is not lost so a second injection is given 1 hour after the first, consisting of 1½ to 3 decimilligrams of Scopolamine without the Morphine according to the patient's condition. Half an hour later the patient's perceptive capacity and memory is tested. This is done by questioning her with regard to memory of the second injection, of any examination which may have been done, or of objects shown to her beforehand. If she remembers things for more than half an hour, she is not sufficiently under the influence of the drug. The memory is thus tested every half hour and further injections are given when memory begins to return. Scopolamine alone is given unless the patient is excited, when Morphine is added. Pain is perceived but immediately forgotten: the condition of the patient is not one of anaesthesia, but of amnesia. After delivery, the patient should wake up remembering * nothing at all about it. This was attained in 80% of the cases. Kronig insists that correct dosing is essential and the test for regulating the dose is that/

that of the patient's ability to remember, nothing else is available. This testing of the memory must be continually carried on and therefore to get perfect results he says "an uninterrupted observation of the patient by trained attendants is imperatively necessary." Better results were got by giving 5 c.c.m. Ethyl Chloride as the head passes the vulva, for this reason, that the last pain caused by the birth of the head is so acute that the partial consciousness of the patient retains it in some cases, and, memory of the pain not being entirely abrogated, the patient believes that the last acute pang is characteristic of the whole course of labour.

Small doses of veronal were also given in some cases to aid the action of the drugs. The patients must be kept quiet and in the dark otherwise Scopolamine tends to induce excitement, and in any case the results are not so good.

In 1700 cases there was not one of circulatory or respiratory disorder as a result, and there was no extra haemorrhage though the blood was measured in all cases. The drugs were given even in cases of organic heart disease with no ill effects. There were two maternal deaths in the whole series, one from/

from haemorrhage with placenta praevia, and one from rupture of the uterus in a contracted pelvis owing to operation being emphatically refused.

If labour is lengthened by the use of this method of producing anaesthesia - and this has not been proved - it is immaterial, half an hour or so, and the relief from pain is worth it.

In 350 cases in private practice in which he used it, he did not need to use "deliverance forceps" once, although the usual average is 40% of cases among the upper classes of Berlin.

With regard to the effect on the infant, he found that 10 per cent were born in a condition of oligopnoea, but breathed on cutaneous stimulation, such as rubbing. There was 1 death intrapartum in 500 cases, and 7 died during the first 3 days, deducting as premature all weighing under 2·500 grams.

Gauss (24) whose paper is based on the first 1000 cases of Kronig's series, states that he had no death due to the drug in that number of cases, although some had heart disease. The duration of labour is said to be increased, but this can be avoided by individualisation of dose. He found that obstetric operations and forceps were not more frequent/

frequent than usual and the results to the children were better than before the introduction of Scopolamine in the treatment of labour. He points out that for parturition only drowsiness and diminished perception is required, and if the dose is regulated accordingly the method is harmless.

Butler (26) reviews Gauss' article and mentions the following statistics:-

In the first 500 cases.

In 451 uterine pains were unaffected

In 8 " " " weaker - due to too much morphine

In 36 " " " stronger

Gauss therefore denies that labour is excessively prolonged, as stated by Hocheisen (27).

In 444 cases the abdominal muscles acted spontaneously

In 16 " " " " " " " when stimulated

In 38 cases the " " " badly.

Three cases had eclampsia, one before injection, but all recovered. The number of forceps cases was 49.

In/

In the Second 500 Cases.

The number of forceps cases was 25, the verdict being that Scopolamine permitted this operation to be avoided when otherwise it would have been necessary. Twenty three had heart disease but none were worse after Scopolamine. No woman died in such a way that blame could be put on Scopolamine in the second 500. One death occurred due to rupture of the uterus. Better results were obtained by excluding morphia from the second dose.

Considering the whole 1000 cases, the percentage of operative cases was the same as in the Berlin clinic, where no Scopolamine was used. Sometimes rapidity and irregularity of the pulse was caused, but not sufficient to cause alarm. No bad results occurred to themothers, beyond a feeling of thirst. Examination of the urine showed that no nephritis was caused. The secretion of milk was unaffected. No dangerous haemorrhage occurred, the average loss of blood being below normal. There was no delay in the third stage of labour, manual extraction being required in only 1 per cent of cases. Disease of the mothers subsequently did not occur in more than the usual number of cases.

With regard to the children, the total mortality in 1000 cases was 29, and before this method was/

was used it was 49. No injury whatever is caused to the child. Of 5 stillborn, one death was due indirectly to Scopolamine because the birth occurred so easily that it was not noticed by the attendants, and the infant was found dead later.

Sometimes the children show a peculiar intoxication especially when the morphine has been repeated. There is slow respiration with cyanosis for 20 minutes or so, if not treated, and then they become normal. The heart slows in the intervals of respiration. At first these infants were treated as if asphyxiated but this was found not to be necessary.

In the first 500 cases, 65 were born asphyxiated, but of these, in 47 other causes were easily found. In 18 no other cause could be found but there was no evidence that it was due to Scopolamine-Morphine. In some cases the mother was not under yet at birth, and in all these no child was intoxicated by Scopolamine. Five children died, two of aspiration pneumonia, two of cerebral injury, and one never breathed. Gauss is certain in the latter case that Scopolamine cannot be blamed for it.

In the second 500 cases the infant mortality was less than during the previous ten years at that clinic, and only half as many were born axphyxiated as/

as in the first 500.

In contrast to the above, Butler (26) gives the experience of Hocheisen (27) whose report was most unfavourable. He had in 100 cases, Postpartum haemorrhage 5 times: 18 children had slow respirations, 15 were asphyxiated, and 1 died - the cause not being stated. His verdict was "Good result usually, but dangerous in private practice." He did not use the memory test, but the reason given by Gauss (25) for his failure was that he used bad preparations of the drugs. Gauss tried a sample of Hocheisen's Scopolamine on 10 patients. He found it was strongly narcotic. On one case it caused deep coma with injury to abdominal and uterine contractions, in 3 cases there was severe post partum haemorrhage, and in 4 strong excitement was caused. Vertigo and vomiting occurred once each, and one child was deeply asphyxiated.

Butler (26) then gives a long list of reports of cases in which Scopolamine was used alone or with Morphine, chloroform or ether, and making no distinction between obstetrical, surgical, or medical cases. This is followed by a list of reports of cases in which Hyoscine hydrobromide 1/100th gr. Morphine sulphate $\frac{1}{4}$ gr. and Cactin 1/67th gr. were used/

used, all the cases being purely obstetrical. The 50 observers mentioned quote 5121 cases with 8 deaths, and two of them with a total of 92 cases give a verdict which is unfavourable.

Summing up, Butler says that the secret of success is the use of good fresh preparations, and small doses with the memory test to regulate the dose. The causes of failure are forcing the effect by too large doses too often repeated, beginning the process too early in labour, or leaving it until there is not sufficient time for its effect to develop, and regulating the dose by the cries of the patient.

A report of 100 cases has been published by Halpenny and Vrooman (9) and their experience has been quite favourable. They gave as the initial dose Scopolamine 1/100th gr. and Morphine ¼ gr., the injection being made when the pains became regular and strong. The subsequent doses consisted of Scopolamine 1/100th gr. alone unless the patient was excited or neurotic, in which case the Morphine was also repeated. They found the effect on the mothers very good, they recovered quickly afterwards and there was no sign of nervous exhaustion following labour. In 20 per cent of their cases, the mother had no memory of the birth: in 25 per cent they gave/

gave a little chloroform just as the head came over the perineum, and in one case forceps were applied without chloroform. They consider that labour is not delayed at all, if anything it is hastened.

Four of the children were born dead: two were premature, labour being induced for eclampsia, one was macerated and one was a posterior position with prolapse of the cord. One needed resuscitation, the mother being a Jewess who had taken absolutely no exercise since the fifth month. The patient, in their opinion, should have a trained attendant, not because of danger, but to ensure that she is left in quiet to get the full benefit of the treatment and because the friends and relatives might be alarmed at the slight mental disturbance, which sometimes occurs.

In summing up they state that they are in accord with Fenton(28) in saying "Do not give the drug within 2 hours of delivery, withhold it after the membranes have ruptured, if there is moderate dilatation of the Os, and when the cervix is completely dilated, even if the membranes be intact. If labour is progressing unusually rapidly, give chloroform instead."

These two writers quote the experiences of several/

several other authors. Fenton (28) with 153 cases, Newell (29) 123 cases, and Kirby (30) give a favourable verdict, the two latter both stating that labour is not prolonged and the patient's strength is conserved by the rest between the pains. Myer (31) in a series of 50 cases found no bad effects on either mother or child. In 6% there was severe haemorrhage and vomiting occurred in two cases. In 46% he got the complete effect, in 42% a fair effect and in 12% no effect.

Regarding the children, in 3 cases there was slight delay in breathing and one was born dead. The latter had a large thymus gland and the cord was wound round the neck. Less favourable reports are given by Steffen (20), who says that he found abdominal pressure was required to aid expulsion, and by Geminder (32) who says that it is dangerous to both mother and child. In 100 cases he met with post partum haemorrhage in five, and the course of labour was disturbed in 27 others. One child died, 11 had serious asphyxia and 12 had slight asphyxia. Sir W.J. Sinclair (33) condemns the method without apparently having had any personal experience of it.

Preller/

Preller (19) used the Scopolamine-Morphine narcosis in 220 cases at the Mannheim lying-in home. His technique was the same as that of Gauss. His initial dose was 1/200th - 1/150th gr. of Scopolamine and 1/8th - 1/16th of Morphine: if this did not cause sleep he gave 1/400th - 1/200 gr. of Scopolamine and 1/20th - 1/16th gr. Morphine, ¾ to 1¼ hours later. Sometimes the Morphine was omitted in the second dose. He found that very rarely were more than two injections necessary, and in no case was more than 1/40th gr. Scopolamine and about ¼ gr. Morphine used for one patient.

In 70% of cases he obtained satisfactory sleep with subsequent oblivion,

In 18%, drowsiness with diminished pain and no oblivion,

In 12%, unsatisfactory results.

The heart's action was unfavourably influenced in 20 - 25% of his cases, as evidenced by acceleration and irregularity of pulse. In such cases he points out that it is better not to give a second dose, or, if one is given, to be very careful. He noticed no injurious effects even with nephritis: the frequency of operative interference was normal, and the third stage in no way influenced. Slight/

Slight toxic symptoms were not uncommon and there was slight delirium and hallucinations in 5%. Lactation was normal. He also states that labour is prolonged in 20 - 30% of cases, owing to the removal of the voluntary action of the abdominal wall, and possibly to diminished force of the uterine contractions as well.

Twenty five per cent of the children breathed badly at first, but rapidly became normal under cutaneous stimulation. One died shortly after birth owing to the forced delivery of the mother for pyrexia.

Preller gives as contra-indications for the use of Scopolamine-Morphine, general debility, serious circulatory and respiratory disorders, primary uterine atony, and secondary as well if due to exhaustion, pyrexial conditions and acute anaemia. In cases of contracted pelvis, premature rupture of membranes and other conditions which prolong labour, the injection should not be given too early.

As a contrast to the favourable opinions expressed by the great majority of the writers quoted up to this point, the experiences of Bertino (34) are marked. He published the results of the use/

use of Scopolamine-Morphine Narcosis in 400 cases. He concludes that the method is dangerous to the foetus, that Scopolamine is unreliable in action, and thinks it should not therefore be used, especially in private practice. In support of these opinions he gives the following figures.

In 36% no analgesic action was apparent and in the majority of cases the pains were attenuated and became irregular - In 38 cases, labour was suspended and retrogressed.

In 14 cases contractions stopped for 2 - 7 hrs.
" 8 " " " 8 - 24 "
" 4 " " " 1 - 2 days.
" 4 " " " 3 - 4 "
" 4 " " " 5 - 6 "
" 2 " " " 10 - 11 "
" 2 " " " 17 - 18 "

He found this was not due to morphine as it occurred even when the dose of this drug was reduced to one fourth of the usual. He obtained the following figures as well.

In 45 % satisfactory result.
" 9.5 % pains weaker and less frequent.
" 36 % no effect apparent.
" 9.5 % labour arrested.

During /

During expulsion patients had to be told to use the abdominal muscles.

26 infants were more or less asphyxiated, but all revived though one died later from respiratory complications. These occurred mostly in the cases in which labour was prolonged.

6 infants died in labour and of these 3 had loops of cord round the neck and one died during extraction with forceps, labour having been arrested for several days after the injection of Scopolamine-Morphine. Thus two are left with no other cause for death, but the great prolongation of the labour following the use of the drug.

In conclusion he stated "In some cases the effect was beneficial, and delivery progressed without any complications, in others the desired effect failed entirely, and in others complications were observed for which the anaesthetic was certainly responsible."

Bad effects were noticed in 70 cases made up as follows:-

Extreme mydriasis and visual disturbance lasting over 24 hours. - - - - - - 56.

Mental confusion, subdelirium, and hallucinations. - - - - - - - - - 10

Obstinate vomiting - - - - - - - - - 4.

One /

One grain of comfort is obtained from the statement that "all his third stages were normal."

Hitherto only the reports of work done in America and on the Continent have been alluded to, but the method has been employed in Great Britain and Ireland as well. At the time Kronig made his address on the subject to the British Medical Association, Buist (35) had done some work on these lines and gave his experience of 65 cases of Scopolamine Morphine Narcosis in Obstetrics.

He gave the first injection when the pains were strong and regular and employed a dose of $\frac{1}{100}$ gr. of Scopolamine and $\frac{1}{6}$ gr. of Morphine, but in private practice he found $\frac{1}{4}$ gr. Morphine more satisfactory. The second dose may be Morphine alone or Hyoscine alone or both together according to the condition of the patient. "If the contractions are really violent, lay stress on the Morphine, if the patient is reacting excessively to what contractions she has, give Scopolamine."

He notes that the uterine contractions were unaffected, the intervals being the same before and after the injection, and in many cases the pains became more regular. One case is quoted in which the pains recurred at 3 minute intervals before /

before injection and afterwards the intervals lessened to 2 minutes.

The 65 cases were made up of 31 primiparae and 34 multiparae. Albuminuria was present in 1 case, Accidental Haemorrhage in 1 case, Accidental Haemorrhage and Pyonephrosis in 1 case, Hyperemesis in 1 case, Mitral Stenosis in 1 case, Aortic Stenosis in 1 case, and Contracted Pelves in 2 cases. Excessive haemorrhage is described in 2 cases during the third stage and in 2 cases post partum, but in the worst case the pulse afterwards was only 96 per minute.

Two children were macerated, all the others alive. Two required artificial respiration, and two stimulation by means of hot and cold baths.

With reference to the use of Scopolamine in private practice, two extracts from his paper may be quoted verbatim, as they are of considerable importance.

"Whenever the patient is distressed by the pains, and you expect the labour to last more than one hour, give an injection of Hyoscine and Morphine. If you expect it to last a considerable time, return in 3 - 4 hours and if necessary, repeat the injection."

"It /

"It is difficult to describe the attractions in private practice of a method which relieves the patient's sufferings while it allows labour to progress regularly, and which does not require the constant personal presence of the medical practitioner as the obstetric anaesthesia with chloroform does."

The next largest number of cases reported upon is that of Professor Sir Halliday Croom, (36) who used this method of obtaining obstetrical anaesthesia in 62 cases, the majority of which I saw and have the privilege of including in this thesis.

The dosage first tried was very small, namely $\frac{1}{400}$ gr. of Scopolamine and $\frac{1}{6}$ gr. of Morphia, the results being disappointing. The chief effect caused was excessive thirst, and there was no loss of consciousness although there was some diminution of the pain felt. The children were quite unaffected.

The dose of Scopolamine was then raised to $\frac{1}{200}$ gr. that of Morphine remaining at $\frac{1}{6}$ gr. with better results. The children were again unaffected and the mothers slept between the pains, the severity of which caused much less evidence of suffering.

Later on the initial dose was raised to $\frac{1}{100}$ gr. of Scopolamine though the same dose of Morphine was still used. In these cases the pain of the contractions of the uterus was perceived still less, /

less, in some cases not at all, and the patients slept soundly between the pains and sometimes through them.

No complaints of thirst were made after the use of the very small dose of Scopolamine was given up. In 37 cases only one injection was required, in 25, the drugs needed repetition in varying doses. The repetition of the Morphia apparently having a greater effect upon the child, to such an extent that ultimately the subsequent injections were confined to Scopolamine alone.

Seventy per cent of the children were vigorous at birth, 27 per cent required slight reviving and 3 per cent needed resuscitation. No children were lost.

Usually the drugs were given in the second stage and never oftener than twice in this stage. The patients usually sleeping for a few hours after completion of labour. In two cases, forceps were applied without the addition of chloroform to the effect of the hypodermic anaesthetics. No bad results were observed on the circulatory or respiratory systems. In 3 cases there seemed to be a tendency to post partum haemorrhage. It was noticed /

noticed that different patients reacted in different degrees to the same dose of the drug, and in one case mental excitement instead of sleep followed the administration of the drugs.

Sir Halliday considers that the patients most suited to this treatment are primiparae of Nervous temperament, especially in private practice, chloroform at the end of the second stage being sufficient in the case of many multiparae.

As far as the labour as a whole is affected, he does not think that the process is either hastened or delayed.

Contra-indications to the use of these drugs are irregularity and feebleness of the pains, and in physical weakness and ill health the case must be carefully watched.

The conclusion Sir Halliday comes to is as follows:- "On the whole, I am of opinion that there can be no question, that in Scopolamine-Morphine Narcosis, we have an efficient means of controlling the pain of labour, and one that is practically safe when ordinary precautions are taken."

Sheill,(2) to whose paper I have already referred, reports observations on 19 cases in Ireland. To half he gave $\frac{1}{200}$ - $\frac{1}{6}$ grs.as the initial dose /

dose and to the rest $\frac{1}{100}$ - $\frac{I}{6}$ gr. To four of the former he gave a second injection of $\frac{1}{200}$ gr. Scopolamine without Morphine, the rest getting only one dose. The first injection is given when the pains become strong and regular. He prefers chloroform for the second stage and does not give Scopolamine-Morphine then. He found that patients stood the second stage better, being less fatigued by a severe first stage. He thinks labour is not shortened, if anything the contrary occurs. A few symptoms, which may disturb both patient and physician, are flushing, dryness of the mouth and thirst, and quickened pulse. None of his patients had delirium, some talked incoherently.

He states that in his experience, if the drug is given within two hours of birth, the patients seem less able or less willing to bear down. He noted a slight inclination for the uterus to relax afterwards. Three of the infants were drowsy. In summing up, he remains uncertain whether the advantages of Scopolamine-Morphine are not outweighed in the majority of cases by certain disadvantages, but admits that it is impossible to decide the question except by observations upon a very large number of cases.

LINES OF INVESTIGATION AND SUMMARY OF RESULTS.

Scopolamine in solution is unreliable unless it is freshly prepared, so, to obviate this difficulty, the drug was used in tabloid form as prepared by Messrs Burroughs and Wellcome. This method is also more adapted to the treatment of extern cases. The Hydrobromide of Hyoscine and Morphine Sulphate were employed, and administered by hypodermic injection, usually directly into the buttock. The dosage varied from $\frac{1}{400}$ gr. to $\frac{1}{100}$ gr. in the case of Scopolamine and from $\frac{1}{6}$ to $\frac{1}{4}$ gr. in the case of Morphine. The larger dose of the latter drug was only used in some 20 cases for the purpose of noting whether the effect on the child became more pronounced. In some cases Scopolamine was given alone, and in others atropine was combined with it and morphine, also for purposes of comparison. In all the rest of the cases, numbering 90, the two drugs were given as nearly as possible according to the methods detailed by Kronig.

The first cases were given very small doses of Scopolamine, namely, $\frac{1}{400}$ gr. with $\frac{1}{6}$ gr. of Morphine. Practically no analgesic action was obtained, the patients/

patients did not fall asleep and one and all complained of severe thirst. Curiously enough, of the large number who were treated with increased doses, hardly one was troubled by thirst. In no case was the birth of the infant or the pain preceding it forgotten. All the children were quite unaffected.

The dose was then raised to $\frac{1}{200}$ gr. Scopolamine the Morphine remaining at $\frac{1}{6}$ gr. with results which were more satisfactory. The patients slept between the pains but wakened up and manifested their suffering during the pains, none complained of thirst and most of them had no memory of the birth of the infant. Only one injection was given as a rule but sometimes it was necessary to repeat the dose after 1 to 1½ hours or longer. The effect upon the children was not bad, the great majority being born in a vigorous condition.

After this the dose was raised further to $\frac{1}{100}$ gr. with the same dose of Morphine as previously used, and the results to the mother were very good. The patients slept soundly between the pains and in some cases through them or only waked up a little during the acme of the pain. In about a third of these cases a further injection was given sometimes with and sometimes without morphia according to the condition/

condition of the patient. The effect upon the children was not so satisfactory as with smaller doses a larger proportion of the children being born in a drowsy condition. In some cases the anaesthesia was sufficient to allow of the application of the forceps without giving chloroform.

An attempt was then made to discover whether the Scopolamine or the Morphine was guilty of causing the foetal intoxication. A number of cases were first treated with Scopolamine alone in varying doses and produced interesting results. The sleep obtained was not so peaceful as in the other cases, there was a greater tendency to excitement and delirium and the analgesia was of less degree. At the same time the condition of amnesia was well developed even when patients had been very noisy. Only one child was drowsy out of eleven.

Then a number of patients were given an injection of Scopolamine $\frac{1}{200}$ or $\frac{1}{100}$ gr. and with it $\frac{1}{4}$ gr. of morphine. As far as the anaesthetic effect was concerned the result was excellent, but a great disadvantage was revealed in the tendency to weaken the uterine contractions and cause them to become irregular. As regards the children the result was startling for 50% were born torpid, and cyanosed.

It/

It was next tried whether the addition of atropine to the dose would do anything to remove these disabilities: $\frac{1}{150}$ gr. of the sulphate was employed in several cases one injection being made. The anaesthetic effect was marked as before but the effects on the children were much the same and the interference with the uterine contractions was present again.

In a few instances the dosage extended to three injections and in some cases the result was extremely satisfactory.

In order to find out whether any influence was exerted by the drug upon the strength and regularity of the uterine contractions a series of observations was carried out as follows. As soon as the uterine contractions became strong and regular the length of the pain and of the interval was counted for 10 consecutive pains. The injection was then made and 45 minutes later 10 more contractions and intervals were timed and compared with the previous 10. This was done in 20 cases picked at random and the result is as follows;-

In 2 cases the pains became weaker and less frequent.

In 16 cases the pains were the same as before

In 2 cases the pains were more severe

Twenty/

Twenty cases is of course too small a number upon which to predicate, but on the whole it appears to me that delay in the progress of labour, which possibly occurs in some cases, is more due to some patients, especially primiparae, ceasing to use their abdominal muscles than to the uterine contractions being weakened. The repetition of Morphia and giving it in the larger dosage of ½ gr. also seems to have an effect the reverse of desirable on the action of the uterus.

GENERAL OBSERVATIONS ON EFFECTS OBTAINED WITH SCOPOLAMINE-MORPHINE.

The effects noticed were thirst in a few cases, drowsiness and sleep, and subsequent oblivion as far as the pains of labour and incidents connected there with are concerned. Of course all cases were not entirely satisfactory or successful for various reasons. In a very few cases flushing of the face was apparent and the patient said her face felt hot. One of two patients stated that they had perceived no difference in the severity of the pain they were suffering, others, also few in number, said the pain became more severe, but the great majority felt the pain relieved and, in some cases, abolished after the injection. Many of those who remembered the birth of the child said it was not painful at all, or that the pain was a mere nothing, their recollection of events prior to the actual birth being very vague and in some cases absent. It was observed that if the patients were kept quiet and undisturbed and the room darkened after injection the effects obtainedwere more satisfactory. This unfortunately was not always attainable, and at times it appeared that when the whole process of labour had been gone through in

a/

a condition of calm sleep the patient was roused into temporary wakefulness by the cries of the infant and thereafter stated that she remembered the birth. In all cases the patient woke up after the sleep, which as a rule succeeded labour, feeling quite fresh. This was particularly remarked upon by multiparae who had had previous experience of the strain of child birth.

One patient suffered from organic heart disease and two from Phthisis Pulmonalis, but neither in their cases nor in any others were any ill effects observed upon the circulatory or respiratory systems.

There seemed to be a little tendency to haemorrhage post partum in a few cases no cause for which could be discovered beyond the influence of the drugs. It was quite easily controlled and was never serious. It was probably caused more by the Morphine than the Scopolamine. Several cases showed symptoms which appeared slightly alarming when first met with, such as excitement and even delirium, one case being almost maniacal. These were easily allayed by a few whiffs of chloroform however, the patient then sleeping quietly. There was never any interference with the process of lactation, and the third stage was always quite normal except in two instances/

instances, one of adherent placenta in a very complicated case and one of retained placenta owing to hourglass contraction of the uterus. In later cases better results were got by giving the patient a few whiffs of chloroform just as the head passed over the perineum,as the acute pain caused by the birth of the head seemed sometimes to penetrate the veil of oblivion which was impervious to the ordinary uterine pains.

Vertigo was never complained of and vomiting occurred in only one patient, who had been in labour for many hours with a contracted pelvis, and who was somewhat exhausted and in addition extremely neurotic. In all cases the pupils were more or less dilated, only in one case was there extreme mydriasis and it did not last for longer than a few hours. No maternal deaths occurred.

It was noticed that when the patient was under the action of Scopolamine-Morphine very little chloroform was required to produce total anaesthesia. For forceps and repairs of the perineum the conjunctival reflex was never lost, but for deeper anaesthesia the absence of pupil indications is at first somewhat confusing. In some cases the application of forceps was carried out without the help of chloroform.

The/

The frequency of operative interference in this series of cases is high for various reasons. The majority of the patients were primiparae owing to the fact that almost all the multiparae when admitted are so far advanced in labour that one cannot be sure that there will be time for the drugs to act before birth takes place. To show how fine the margin of time many multiparae allow it may be mentioned that in 6 months, 3 children were born in the street, and 3 in cabs on the way to the hospital, one in the entrance hall and 5 in the receiving room before the patient was undressed. Married woman also by far prefer to be confined in their own homes and in many cases only enter hospital when the labour becomes complicated. On the other hand unmarried girls, by the regulationsof the institution are not treated unless they are admitted to the wards, and as the vast majority of them are primiparae the list of forceps cases is thereby swelled. One more reason may be brought forward to account for the high number of operative cases, and that is, that the hospital taps a large district from which practically all the cases it receives are anything but normal labours.

One of the most important questions with regard to the action of Scopolamine is its effect on the/

the duration of labour. In two or three cases the uterine contractions definitely ceased after injection but two of these were complicated cases and the drug cannot be specifically blamed. It is of course impossible to foretell the length of time that any particular labour will last, hence the difficulty of deciding whether it is prolonged, unaffected, or shortened by scopolamine. It can only remain a matter of opinion without careful observation and timing of a very large number of confinements. In some cases it apparently hastens the process, as witness the case noted by Sir Halliday Croom,, in which the os dilated to its full extent in two hours. If it does delay the progress of parturition at all it has seemed to me to be of so little account on the whole that it is fully compensated for by the other advantages which the drug confers.

The first injection was usually made well on in the first stage or early in the second stage, the effect being noticeable in about half an hour, sometimes in less than that time, the dose being repeated or a smaller one given if necessary, an hour or more after the first injection. The best method of discovering when a second administration is required is the memory test as used by Gauss. Better results,/

results, especially to the children, were noticed when the morphine was not repeated. The best indication for giving a second dose of the latter drug is the presence of excitement or a tendency to it.

With regard to the effects on the children a tendency to cause a peculiar somnolent condition is very evident, especially if the dose of morphia has been large or given late on in labour. The infant appears to be too sleepy to exert itself to the extent of crying or breathing vigorously for the first 30 minutes of its existence, more or less, and during this time the face is cyanosed as a rule. It then becomes normal and often sleeps for some time. In some cases resuscitation is necessary even to the extent of artificial respiration but as a rule vigorous smacking and alternate hot and cold baths are sufficient to wake it up. The number born dead is rather large but in no case can Scopolamine-morphine be blamed for causing death, the cases in which the infant was not premature being all complicated by some abnormity of labour. The large number of complicated cases in itself suggests a high foetal mortality rate.

TABLE I. SMALL DOSES OF SCOPOLAMINE AND OF MORPHINE.

	A	B	C
Number of cases (Primipare.2, Multiparae 4).	4	1	1
Number of Injections	1	2	2
Dosage.	1/400+1/6	(i) 1/400+1/6 (ii) 1/400	(i) 1/400+1/6 (ii) 1/400+1/6
Effect on Mother, Slept	-	-	-
No effect except Thirst	4	1	1
Excited	-	-	-
Delirious	-	-	-
Memory. Remembers Birth.	4	1	-
No memory of birth.	-	-	1
No difference to pain	-	-	-
Pain increased	-	-	-
Pain diminished	4	1	1
Effect on Child - Lively	4	1	-
Drowsy	-	-	-
Resuscitated	-	-	-
Dead	-	-	1
Chloroform given for Forceps	-	-	1
" " " other operations	-	-	1
Forceps cases	-	-	1
Complicated cases	-	-	1

COMMENTS:- Evidently the dose of the drug was not sufficient to produce the desired effect. All these patients complained of excessive thirst, a symptom almost entirely absent when larger doses were used. None of these patients slept after Scopolamine, but all were slightly drowsy and stated that the pain of the uterine contractions was slightly diminished, although both these and the birth of the child were remembered.

The case in series C. was one of severe Accouchement Forcé. Chloroform was given for birth with forceps but the patient remembers the pain previous to that and also getting the mask for the general anaesthetic.

TABLE II. MEDIUM DOSE OF SCOPOLAMINE AND SMALL DOSE OF MORPHINE.

Number of cases (Primiparae 7 Multiparae 9)	16
Number of Injections	1
Dosage	$\frac{1}{200}+\frac{1}{6}$
Effect on Mother - Slept.	15
No effect	-
Excited	1
Delirious	-
Memory. Remembers birth	3
No memory of birth	13
No difference to pain	-
Pain increased	1
Pain diminished	15
Effect on Child - Lively	15
Drowsy	-
Resuscitated	-
Dead	1
Chloroform for Forceps	3
" " Other operations	1
Forceps cases	4
Complicated cases	3

COMMENTS:- One of these patients on whom the drugs had the usual effect has already been referred to as remembering nothing of her first labour a year ago under the hypodermic anaesthetic above. She states that she remembers the birth of this child, but the pain was of so small a degree that she thinks nothing of it. The case of the one woman that became excited after injection was complicated by Accidental and Post Partum Haemorrhage, though the latter was not severe. In one case after delivery - next day - the patient said the pains were more severe after injection but at the same time she did not remember the birth and had a very hazy idea of the two hours which intervened between that event and the receiving of the dose. She slept calmly all the time without a sound. Four patients were delivered with forceps, in one case without chloroform: of those who had chloroform one case was a posterior position which underwent short rotation, the child also being an exceptionally large one. All the children were lively at birth except one born dead - indeed not viable - the result of an accouchement forcé, the only other/

other operation besides forceps. The three complicated cases were one accidental haemorrhage and one face to pubis case, both mentioned above and one R.O.P. case which underwent long rotation and in which the cervix was torn and bled a good deal.

TABLE III. MEDIUM DOSE OF SCOPOLAMINE AND SMALL DOSE OF MORPHINE REPEATED WITH OR WITHOUT MORPHINE.

	A.	B.
Number of cases (Primiparae 2 Multiparae 1).	1	2
Number of Injections	2	2
Dosage.	(i) 1/200+1/6 (ii) 1/200+1/6	(i) 1/200+1/6 (ii) 1/200
Effect on Mother - Slept.	1	2
No effect	-	-
Excited	-	-
Delirious	-	-
Memory. Remembers birth.	-	-
No memory of birth	1	2
No difference to pain	-	-
Pain increased	-	-
Pain diminished	1	2
Effect on Child. Lively	-	-
Drowsy	-	2
Resuscitated	1	-
Dead	-	-
Chloroform for Forceps	1	-
" " Other operations	-	-
Forceps cases	1	1
Complicated cases	1	-

COMMENTS:- The case in series A was most complicated. The woman was hemiplegic one side being almost paralysed entirely, the presentation was a vertex R.O.P., the cervix was indurated and required digital dilatation, she had had 6 children previously and it came out later had had Post Partum Haemorrhage more or less severe with every one of them. She was ultimately delivered with forceps under chloroform, the placenta was adherent and had to be manually removed while she concluded her labour with a very severe Post Partum Haemorrhage. Both she and the child survived but the latter required resuscitation.

One case in series B. required forceps for delivery this being accomplished without the aid of chloroform. Both children were drowsy and one lived only 12 hours. It was premature and very small and feeble.

TABLE IV. LARGE DOSE OF SCOPOLAMINE AND SMALL DOSE OF MORPHINE.

Number of cases (Primiparae 22 Multiparae 26)	48
Number of Injections	1
Dosage	$\frac{1}{100} + \frac{1}{6}$
Effect on Mother. Slept	44
No effect	1
Excited	3
Delirious	-
Memory - Remembers birth	7
No memory of birth	41
No difference to pain	3
Pain increased	1
Pain diminished	44
Effect on Child - Lively	36*
Drowsy	4
Resuscitated	7
Dead	2
Chloroform given for Forceps	9
" " " Other operations	1
Forceps cases	9
Complicated cases.	8

*Including twins.

COMMENTS:- One patient had a hazy recollection of the birth while in the hospital but after a second labour a year afterwards she said she remembered nothing of the first labour which was quite painless as she had had chloroform! She really had only Scopolamine and Morphine. In one case the pains became weaker and infrequent and then stopped for 1½ hours when they returned gradually at first but never became as strong as they were before the injection. She was ultimately delivered with forceps. The child was quite vigorous. Of the 3 cases which became excited after the administration of the drug one was a chronic alcoholic who had been previously treated for Hyperemesis Gravidarum and discharged cured. She returned in labour, intoxicated (which she had been for 3 days) and covered with bruises. The child was premature very feeble and had to be resuscitated: it lived only 6 hours. The presentation was a Breech. This patient and one other of the 3 had no memory of the birth. The one patient on whom the drugs had no effect said the pains were worse after/

after the injection and she remembered every thing distinctly. Three patients said the injection caused no difference in the pain felt, all three remembered the birth and in two of them the pains were unusually violent.

Forceps were used 9 times always with chloroform, only a few whiffs being necessary and the conjunctival reflex was never lost in any of the cases. Chloroform was given in one other case in which operative interference became necessary namely an L.O.P., position in a justo-minor pelvis when crainotomy had to be performed.

The 8 cases of complication were as follows:-

Two cases of Accidental Haemorrhage.

One case of Hour-glass contraction of the uterus retaining the detached placenta and causing severe haemorrhage in the third stage. The placenta was manually removed and the uterus contracted at once and all bleeding ceased.

One case of enormous ventral hernia in an old appendectomy scar. The child was born with the help of forceps the occiput having rotated into the hollow of the sacrum.

One/

One case of Face Presentation in which the mother had eclamptic fits beginning $7\frac{1}{2}$ hours after delivery.

One case of Chorea Gravidarum: the movements being controlled by the drugs.

One case of oedema of the cervix, in which labour lasted 40 hours and the child, weighing just under 11 lbs., was born dead.

One case of generally contracted pelvis referred to above.

With regard to the children some interesting points may be mentioned. Of those who were born vigorous one lived only 2 days, during which time it had one or two convulsions; an autopsy showed the lateral sinus ruptured in 3 places with resulting intracranial haemorrhage (Forceps were not used in this case): one had a spina bifida and club feet and developed a congenital laryngeal stridor some hours after birth; the presentation was a Breech. Of those, born in a torpid and drowsy condition 2 were brought over the perineum with forceps and another was the child of one of the women described above who had such unusually violent pains. Seven children needed resuscitation/

resuscitation. Two of three were premature and lived for under 6 hours while in other two the apnoea was explained by the presence of a lump of vernix caseosa blood and mucus in the throat. This having been removed they were soon all right. The two infants born dead were the children of the last two women mentioned in the list of complicated cases.

Those infants born drowsy needed very slight stimulation to start them breathing, a slight smack or two being quite sufficient. At first they were regularly resuscitated and noted as requiring such, hence the somewhat large number under this heading, but afterwards it was found that this was not necessary.

TABLE V. LARGE DOSE OF SCOPOLAMINE AND SMALL DOSE OF MORPHINE WITH VARIOUS DOSES OF SCOPOLAMINE REPEATED, WITH OR WITHOUT MORPHINE.

	A.	B.	C.	D.
Number of cases (Primiparae 10 Multiparae 5).	4	2	4	5
Number of Injections	2	2	2	2
Dosage	(i) 1/100+1/6	(i) 1/100+1/6	(i) 1/100+1/6	(i) 1/100+1/6
	(ii) 1/200	(ii) 1/200+1/6	(ii) 1/100	(ii) 1/100+1/6
Effect on Mother Slept	4	1	4	3
No effect	-	-	-	-
Excited	-	-	-	-
Delirious	-	1	-	2
Memory Remembers birth	1	-	-	-
No memory of birth	3	2	4	5
No difference to pain	-	-	-	-
Pain increased	-	-	-	-
Pain diminished	4	2	4	5
Effect on child. Lively	3	1	1	3
Drowsy	-	-	1	-
Resuscitated	1	-	2	1
Dead	-	1	-	1
Chloroform for Forceps	1	-	1	2
" " Other operations	-	-	-	1
Forceps cases	1	1	2	2
Complicated cases.	1	1	-	1

COMMENTS:- The only patient who said she remembered the actual birth of her child had a very vague idea of what happened, and as she had had seven babies previous to this one it is very probable that her recollection was largely due to imagination helped no doubt by memories of previous labours. Of the three who became delirious the one in series B was affected at first but calmed down after the second injection while the remaining two in series D. only became delirious after the second injection. Both the latter required forceps for delivery and were given chloroform. There were four other forceps deliveries two of these being done without chloroform namely one in series C, and one in series B, in the case of the woman who was delirious after the first injection. Chloroform was given in one other case, in series C, where a brow presentation was turned to a vertex. Of the three cases with complications that in series A. was a case of flat pelvis where premature labour was induced, that in series B, was a case of advanced pulmonary tuberculosis/

tuberculosis in which premature labour was induced before the seventh month and the third, in series D, was an old multipara who had had 12 children already. She went into labour at the 7th month and had an extremely indurated and undilatable cervix. The first stage lasted about a week the woman having strong and regular pains at intervals of 3 to 5 minutes several times for hours at a time. During this time she had 3 or 4 injections of morphia before the cervix dilated sufficiently to allow labour to progress.

Coming now to the children it will be seen that two of these were born dead, both being premature. Four required resuscitation, one being a forceps case, one an R.O.P. position which rotated to R.O.A., the labour being somewhat prolonged, and one was premature and lived only 5 hours the mother being the complicated case in series D. Of those born in a lively condition one was premature but lived and was discharged with the mother, and one died the day after its birth. This infant was premature and had a depressed fracture of the cranium, the mother/

mother having had premature labour induced for a flat pelvis. A Post Mortem examination revealed a large subdural haemorrhage.

The presentation was a breech.

TABLE VI. SCOPOLAMINE ALONE.

	A.	B.	C.
Number of cases (Primiparae 6 Multiparae 5).	3	7	1
Number of Injections	1	1	2
Dosage	1/200	1/100	(i) 1/100 (ii) 1/200
Effect on Mother. Slept	2	6	-
No effect	-	-	-
Excited	1	1	-
Delirious	-	-	1
Memory. Remembers birth	1	2	-
No memory of birth	2	5	1
No difference to pain.	-	-	-
Pain increased	-	-	-
Pain diminished	3	7	1
Effect on child. Lively	3	6	1
Drowsy	-	1	-
Resuscitated	-	-	-
Dead	-	-	-
Chloroform given for Forceps	-	-	-
" " " Other operations	-	-	-
Forceps cases	-	-	-
Complicated cases	-	-	-

COMMENTS:- In all these cases the sleep produced was not so calm and restful as that obtained by the combination of Morphine with the Scopolamine, while in 3 cases out of the 11 the patient did not sleep but became excited and in one case delirious. The after memory of the birth and pains seems to be as blurred and vague as when morphine is given in spite of the excited condition while under the action of the drug. In the case in series A. in which the birth is remembered the child was born too soon after the injection for the drug to take effect. One of the children in series B., was a breech but was very vigorous. The case in series C., was quite delirious and had to be given chloroform to keep her quiet, only a few whiffs being necessary: the pupils were very widely dilated but there were no ill effects observable on the respiration or circulation. As soon as the infant was born she fell into a deep sleep which lasted some hours and woke up feeling very fresh.

TABLE VII. VARIOUS DOSES OF SCOPOLAMINE AND LARGE DOSE OF MORPHINE.

	A.	B.
Number of cases (Primiparae 11 Multiparae 2)	7	6
Number of Injections	1	1
Dosage	1/200+$\frac{1}{4}$	1/100+$\frac{1}{4}$
Effect on Mother. Slept	7	6
No effect	-	-
Excited	-	-
Delirious	-	-
Memory. Remembers birth	2	1
No memory of birth	5	5
No difference to pain	-	-
Pain increased	-	-
Pain diminished	7	6
Effect on Child. Lively	2	1
Drowsy	2	2
Resuscitated	2	1
Dead	1	2
Chloroform for Forceps	-	-
" " Other operations	-	-
Forceps cases	-	-
Complicated cases.	-	-

COMMENTS:- In all three cases in which the birth of the child was remembered that event took place so long after the administration of the drugs that their effect had time to wear off. The three children born dead were all premature, two of them being macerated.

In one case in series B., the pains became markedly weaker and less frequent after the injection.

TABLE VIII. MEDIUM DOSE OF SCOPOLAMINE AND LARGE DOSE OF MORPHINE COMBINED WITH ATROPINE.

Number of cases (Primiparae 3 Multiparae 3)		6
Number of Injections		1
Dosage		$\frac{1}{200}+\frac{1}{4}+\frac{1}{150}$
Effect on Mother.	Slept	6
	No effect	-
	Excited	-
	Delirious	-
	Memory. Remembers birth	2
	No memory of birth	4
	No difference to pain	-
	Pain increased	-
	Pain diminished	6
Effect on child.	Lively	4
	Drowsy	1
	Resuscitated	1
	Dead	-
Chloroform given for Forceps		1
" " " Other operations		-
Forceps cases		1
Complicated cases		-

COMMENTS:- In two cases the pains became markedly infrequent and weak after the injection and in one of these the child had to be resuscitated. One of the children which were vigorous at birth died 17½ hours later and an autopsy disclosed the cause of death as atelectasis. One woman required forceps for delivery for which operation she had a few whiffs of chloroform.

MISCELLANEOUS CASES

Total 8 (Primiparae 6 - Multiparae 2.)

1. Two cases. Two injections each with morphine alone in the second injection.

(a.) $\frac{1}{100} + \frac{1}{6}$ with $\frac{1}{4}$ gr. of Morphine repeated 4 hours later. On admission the presentation was a brow and the os was three fourths dilated. The head was caught at the brim of the pelvis and the pains were weak and infrequent. The patient was very weary having been in labour for many hours. After the initial dose she slept undisturbed for $3\frac{1}{2}$ hours when she woke. No progress had been made but the os was now fully dilated. Chloroform was given and the head flexed, it now taking the R.O.P. position, with vertex presentation. The woman was still very weary and the pains almost absent, so she was given $\frac{1}{4}$ gr. of Morphine and put to bed, where she slept peacefully for 5 hours. She then woke with a pain and after 3 or 4 more good strong pains, the infant was born in a vigorous condition without any trouble. She had a very hazy remembrance of the birth of the child.

(b.) /

(b.) $\frac{1}{100} + \frac{1}{6}$ with $\frac{1}{6}$ gr. Morphine 3 hours later. After the initial administration, the usual effect was obtained at first but later she became somewhat excited, so $\frac{1}{6}$ gr. Morphine was given 3 hours after the first injection. She became quite quiet and the pains were unaltered in strength or frequency but she made no progress, so was delivered with forceps, a few whiffs of chloroform being given. The baby was vigorous. She remembers getting the mask for the general anaesthetic, and the pains, but states the latter were very greatly relieved by the injections.

2. One case. Three injections, each of $\frac{1}{100} + \frac{1}{6}$. In this case the presentation was vertex in the right posterior position. The membranes ruptured almost with the first pain, resulting in a dry labour, the os being very slow in dilating. The first two injections were given at 8 40 p.m. and 11 50 p.m. on the 16th. The pains became weak and infrequent and she slept soundly. 10 hours later, on 17th, the pains returned strongly and regularly and she had the 3rd hypodermic. She slept again and the pains ceased entirely till the next /

next day, the 18th, when they returned,no more Scopolamine was given but she was delivered by forceps with chloroform. The infant was quite vigorous. She remembers of course all that happened after she recovered from the effects of the third injection. She says the pains were entirely relieved by the Scopolamine.

(3.) One case. Three injections. $\frac{1}{100} + \frac{1}{6}$ followed after 8 hours by $\frac{1}{200} - \frac{1}{6}$ and 3 hours later $\frac{1}{200}$ without morphine. This case was one of the most successful. The patient was under the influence of Scopolamine for 14 hours, the pains being relieved without losing either in strength or frequency and the woman sleeping quite peacefully. Ultimately she was delivered with forceps, no chloroform being used and the child being born as lively as possible. She remembers nothing after the first injection, and would not believe that she had a baby to call her very own until it was produced as proof that she had been delivered. She was a primipara and /

and felt fresh enough after the labour to get up and walk home.

(4.) One case. Three injections. $\frac{1}{100} + \frac{1}{6}$ repeated after 4 hours and 3 hours after that $\frac{1}{200}$. This case resembled the previous one except that forceps were not used. In all other respects they are similar.

(5.) One case. Three injections. $\frac{1}{100} + \frac{1}{6}$ followed after an hour by $\frac{1}{200}$ and $1\frac{1}{2}$ hours after the second by $\frac{1}{400}$, The usual effect was obtained after injection but wore off much sooner than usual after the 3rd dose. The child was lively. She remembers the birth in a vague way but had no pain.

(6.) One case. Three injections. $\frac{1}{100} + \frac{1}{6}$ and $\frac{-1}{200}$ and $\frac{1}{6}$. The first injection had no effect so the second was given an hour later. This too had but little result, so $\frac{3}{4}$ hour later $\frac{1}{6}$ gr. of Morphine was given after which she lay very quiet, bearing down well. The baby was born 40 minutes later and was drowsy. The mother's recollection is hazy up to the birth which is distinct and painful.

(7.) One /

(7.) One case. Three injections. $\frac{1}{100} + \frac{1}{6}$ and $\frac{1}{200}$ and $\frac{1}{100} - \frac{1}{6}$. This case is somewhat complicated. The patient was an epileptic, having frequent severe fits and was distinctly weak mentally. Premature labour was induced by Krause's method and when the pains became strong and regular she had $\frac{1}{100} + \frac{1}{6}$ with the usual good effect, which lasted for $2\frac{1}{2}$ hours. She then had $\frac{1}{200}$ gr. Scopolamine alone and 2 hours later the pains ceased, the os being the size of a florin. Four hours after this the pains returned regularly every 3 - 4 minutes and she became very noisy and alarmed, so was given $\frac{1}{100} + \frac{1}{6}$ with the usual soporific effect, the pains being unaffected in strength or frequency. Before birth the action of the drugs seemed to have passed off to a large extent, but though she remembered the birth, she said it was not painful. The child was lively. Seen a year later after her second confiement, she stated that this one - the first - was painful, more so than the second. Her intelligence was not such, however, that much reliance could be placed upon it. The presentation in this case was a vertex in the right posterior position.

TABLE IX. TOTAL RESULTS ON 126 CASES, WITH PERCENTAGES.

		NUMBER	PERCENTAGE
Total number of cases		126	-
	Primiparae	69	54·7
	Multiparae	57	45·2
Number of Injections		1 to 3	-
Range of Dose.	Scopolamine	$\frac{1}{400}$ to $\frac{1}{100}$	-
	Morphine	$\frac{1}{6}$ to $\frac{1}{4}$	-
Effect on Mother.	Slept	108	85·7
	No effect	8	6·3
	Excited	6	4·7
	Delirious	4	3·1
	Memory. Birth remembered.	28	22·2
	Birth not remembered.	98	77·7
	No difference to pains	3	2·3
	Pain increased	2	1·5
	Pain diminished	121	96·0
Effect on Child.	Lively	*88	69·8
	Drowsy	14	11·1
	Resuscitated	16	12·6
	Dead	9	6·9
Forceps cases.	Total	26	20·6
	With chloroform	21	16·6
	Without chloroform	5	3·9
Complicated cases		19	15·0

* Including Twins.

ANALYSIS OF TOTAL NUMBER OF CASES.

On referring to Table IX., it will be seen that the majority of the patients were primiparae which partly accounts for the rather large number of cases in which forceps was required.

The percentage of successful cases, that is to say, those in which there was no recollection of the birth of the infant, reached 77·7 which is high compared with the experiences of others. This is partly explained by the fact that several had choloform for delivery, either by forceps or naturally, in the latter case a few inhalations being quite sufficient just as the head passes the vulva.

In practically every case the pain was lessened even though complete amnesia was not obtained.

Of the 28 cases in which birth was remembered, 6 were due to the dose being too small. They are the cases in Table I. Four were unsatisfactory because the child was born before the drug could take effect and other four failed because the effect wore off before birth and yet it did not seem wise to give another injection as the head/

head might have been born at any moment. This leaves only 14 failures really due to lack of the usual action of the drug.

Among the children vigorous at birth there was one pair of twins. Three died within 3 days and of these one lived 2 days and had two convulsions the cause of death being introcranial haemorrhage, one died the day after birth: it was premature and had a depressed cranial fracture, one lived 17½ hours the cause of death being atelectasis.

Sixteen children were resuscitated and four of these died within 3 days all being premature. Of those born in a drowsy condition one died after 12 hours. It was very small and feeble and was premature.

Nine children were born dead, one the result of craniotomy, one, a very large child, after a prolonged labour due to oedema of the cernix, seven were premature: two of these died before birth and were macerated, and other two died as the result of operations for accouchement forcé.

Five cases were delivered with forceps, without chloroform being necessary.

TABLE X. RESULTS AND PERCENTAGES ON 90 NONEXPERIMENTAL CASES.

	NUMBERS	PERCENTAGE.
Number of cases	90	
Primiparae	47	52·2
Multiparae	43	47·7
Number of Injections	1 to 3	
Range of Dose(Scopolamine	$\frac{1}{200}$ to $\frac{1}{100}$	
(Morphine	$\frac{1}{6}$ to $\frac{1}{4}$	
Effect on Mother. Slept	81	90·0
No effect	2	2·2
Excited	4	4·4
Delirious	3	3·3
Memory. Birth remembered	16	17·7
Birth not remembered	74	82·2
No difference to pain	3	3·3
Pain increased	2	2·2
Pain diminished	85	94·4
Effect on child. Lively	66*	73·3
Drowsy	8	8·8
Resuscitated	12	13·3
Dead.	5	5·5
Forceps cases. Total	24	26·6
With chloroform	19	21·1
Without chloroform	5	5·5
Complicated cases	17	18·8

* Including twins.

NOTES ON TABLE X.

It will be seen that satisfactory results were obtained in a higher percentage of cases in the series which excludes all the cases which were experimental in character. The latter are included in Tables I. VI. VII. VIII.

There is not much difference between the two last tables as far as complications are concerned but the percentage of forceps cases is a good deal higher in the nonexperimental cases although the comparative numbers of primiparae and multiparae approximate a little closer to each other.

The foetal mortality rate is lower and the number of children born in a vigorous condition is greater comparatively than in the total number of cases. The percentage of children drowsy at birth is smaller though a slightly greater percentage of infants required resuscitation.

S U M M A R Y.

ADVANTAGES AND DISADVANTAGES.

In the foregoing series of cases it has been seen that there are both advantages and disadvantages in the use of Scopolamine in labour. The advantages conferred by the use of the drug on the mother are very great; the total relief of pain and anxiety obtained in the successful cases being a boon the value of which it is not easy to estimate. And we have seen that in skilled and experienced hands the number of completely successful cases reaches 80%. The advantages obtained by its use are not confined entirely to the patient. It is a help to the busy practitioner in the conduct of his work for he is able to produce an analgesia for his patient without having to be constantly present in person to administer chloroform or other anaesthetic during the pains. This too will assist him in the face of relatives and patient who are impatient and anxious and possibly losing faith in his skill because they are unable to understand that labour is a process/

process which must take its own time to pass through stages of preparation and expulsion and cannot be brought to a speedy end by some simple manoeuvre comparable to drawing a tooth. The sight of the patient calmly sleeping through the pains is bound to have a reassuring effect on the relatives and friends. The freedom from exhaustion which follows its use is a powerful argument in its favour and I have noticed again and again that multiparous patients have mentioned this even before the diminution of the pain or its abolition in describing the differences between labours with and without Scopolamine.

In short then, its advantage is that the pain of labour is robbed of its terror and the fatigue and exhaustion which follow confinement are abolished in the great majority of cases.

To turn to the disadvantages of the method and compare them with the foregoing statements. The list of reasons why the drug should not be used is a long one but none of the disadvantages urged against the drug are insurmountable. In the first place in a small percentage of cases the result is the opposite of that expected and the patient becomes excited and incoherent. This condition need cause no/

no alarm however and as a rule is overcome by a few inhalations of chloroform or by a slight increase in the dose of Morphine. The occurrence of thirst and flushing is rare and causes but little inconvenience a mere nothing when compared to the actual pain of labour. Some observers contend that the sleep which usually follows the completion of delivery is a disadvantage but I fail to see that this is so and I consider it one of the beneficent actions of the drug as the patient invariably wakes up much refreshed and in a large number of cases, to her surprise, meets with the cheering news that her troubles are over and that the cause and reward of them is sleeping peacefully in the cot at her side.

The chief argument against the use of Scopolamine would seem to be the effect upon the child, but I think that the experiments in dosage with the Morphine part of the treatment has shown pretty conclusively that the torpor of the babe is due to the latter drug. Careful individualisation of the dose and the non repetition of the dose of morphine whenever possible, will do much to remove this objection. Of course the more experienced the practitioner becomes in the use of the drug the better the results he will achieve. It will be noted that in the whole/

whole 126 cases no maternal death occurred and no foetal death could be attributed to the use of Scopolamine-morphine in spite of the large percentage of complicated cases.

With regard to the assertion that labour is prolonged, in my experience, except in one or two cases, this was not proved to occur and when it did, I am not sure that the evidence is conclusive that the blame attaches to the use of Scopolamine-morphine. This is a question which can only be settled by very careful observation of a large number of cases. If labour is prolonged by it I do not think that a difference of more than half an hour on an average is caused. And if it is, surely the relief from pain and anxiety is worth the extra time.

Its use in private practice is bound to be more restricted than in hospital, owing to the fact that an attendant intelligent enough to understand and carry out directions regarding the patient while the latter is under the influence of the drug is not always at hand. Without such an attendant the use of the narcotic might be attended by danger.

Personally I have never seen any ill effects upon pulse, heart, or respiration follow its use: nor has there been any harmful influence upon the/

the third stage or the puerperium.

Looking back upon these observations on the advantages and disadvantages of the drug, the list of the latter appears - and is - more extended than the former but I do not consider that the advantages of its use are outweighed.

DOSAGE AND ADMINISTRATION.

The best time to give the initial dose is when the pains become regular with intervals of about five minutes, the amount depends upon the condition of the patient, the extent of the reaction to the pain, the stage of labour reached and so on. Of course if it appeared probable that the child would be born before the effect of the drug could be developed, it would be better to withhold Scopolamine-morphine altogether, for chloroform would be more satisfactory for the short time remaining in which anaesthesia would be desirable.

As regards the dose I think it is impossible to lay down a hard and fast rule. It is bound to vary. Under most circumstances I consider 1/200 gr with 1/6gr. of Morphine a good dose to begin with, and if necessary it can be repeated with or/

or without Morphine in $\frac{3}{4}$ to $1\frac{1}{2}$ hours. The repetition of dose is best regulated - indeed can only be regulated - by the reaction of the patient to the memory test. The earlier in labour that the time arrives to give the hypodermic, the bigger may the dose be, but it should never exceed $^{1}/_{100}$gr., and repeat doses are usually better to be kept at $^{1}/_{200}$gr. I have found the best way to give the drug was to dissolve the tabloids in the requisite amount of distilled sterilised water in a hypodermic syringe, and after cleansing the skin with ether, to plunge the needle straight into the buttock or upper part of the thigh, during a pain. Under these conditions the patient hardly notices the administration.

To obtain the best results the patient should then be kept quiet and undisturbed in a darkened room. I did not plug the ears with wool according to the Freiburg method but I think that this would be of benefit.

In this series of cases the results were quite good in support of which contention I may be allowed to quote a few figures from Table IX.

85·7% slept peacefully after the injection.

77·7% had no recollection of the birth of the infant.

96·0%/

96·0% declared the pain was diminished or abolished

69·8% of the children were vigorous

11·1% " " " drowsy

12·6% " " required resuscitation

$\frac{1}{5}$ of the forceps cases were delivered without chloroform.

The results obtained in the series of 90 cases in which no experiments were tried with the dosage of morphine were better in many respects.

Several infants are classed as "resuscitated" which should only be among the number of those born drowsy, owing to the fact that at first the drowsy ones were subjected to methods of resuscitation which were afterwards found to be unnecessary.

C O N C L U S I O N.

In conclusion I may state that I consider this method of producing anaesthesia in both normal and abnormal cases of labour to be a very valuable addition to the science of Obstetrics.

Although to obtain perfect results the patient should be under strict and trained medical observation/

observation such as obtains only in an hospital or in the best class of private practice, still I am of opinion that it may be of enormous help to the busy medical man in all classes of practice, and the more each individual observer uses the method the better the results he will obtain, for he will learn to discriminate between those cases which are likely to be benefited and those which are not.

With regard to the safety of the procedure, as far as the mothers are concerned, I do not think that with ordinary care there is any danger to be feared except in very exceptional cases. In the case of the children, perhaps there is an element of danger, but I have never seen a case in which the child did not quickly respond to the ordinary methods of resuscitation even in the severest cases of intoxication. But I consider that care in the use of the morphine element of the treatment especially within an hour or two of birth will practically abolish any risk there may be. The dosage of Scopolamine also should not be too heroic towards the latter end of labour.

To obtain the best results care should be taken to use only drugs which are carefully and reliably standardised as to dosage otherwise the effects caused will vary within very wide limits.

B I B L I O G R A P H Y.

1. CUSHNY. Pharmacology p. 276.289.290.
2. SHEILL. Pract. 1910 Feb.
3. B.P. (last ed.)
4. HARE. Therapeutics p. 430.
5. BRUCE. Mat. Med. and Therap. p. 362.
6. LANPHEAR. Lancet 1907 II p. 976. abstr. from Internat. J. of Surg. and J. Surg. Gynec. and Obst. N.Y. 1907 XXIX p. 347 - 351.
7. JAMIESON. B.M.J. 1910 I p. 742.
8. MOORE. Lancet 1907 I p. 1084.
9. HALPENNY. and VROOMAN) Am. J. Obst. N.Y. 1909 LX.p.611-620
10. STELLA. Archiv. de Pharmacodinamie et de Therap. T III. 1897.
11. KOCHMANN. Archiv. de Pharmacodinamie Bd. XII. 1904
12. WEBSTER. J. Winnipeg Med. Chir. Soc. 1906-1908 p83.
13. LEEDHAM-GREEN. B.M.J. 1909 II p. 962.
14. NICHOLSON. J. Am. Med. Ass. 1909 April.
15. SCHNEIDERLIN. Aerzliche Mitteilungen aus und für Baden 1900 Mai.
16. KORFF. Munch. Med. Woch. 1901 No. 29. Ibid 1902 No. 27.

17./

17. BLOS. Beitrage zur Klin. Chirurg. Bd. XXXV Heft 3

18. STEINBUCHEL. Centralbl. f. Gynäk. 1902 No. 48.

19. PRELLER. Munch. Med. Woch. 1907 LIV. p. 161.

20. STEFFEN. Archiv. f. Gynäk. LXXXI 1907 No. 2.
abstr. in J. Am. Med. Ass. 1907
May p. 1821.

21. LEOPOLD. Archiv. f. Gynäk. Bd. LXXXI Heft 3.

22. Bass. Munch. Med. Woch. 1907 No. 11.

23. KRONIG. B.M.J. 1908 II p. 805 - 808.

24. GAUSS. Munch. Med. Woch. 1907 LIV p. 157.

25. KRONIG und GAUSS. Ibid. 1907 No. 40 and 41.

26. BUTLER. Am. J. Obst. N.Y. 1907 LVI p. 171 - 177.

27. HOCHEISEN. Munch. Med. Woch. 1907. No. 11.

28. FENTON. Canad. J. of M. and S. 1907.

29. NEWELL. Surg. Gynäc. and Obst. 1907 Aug. abstr.
in Am. J. Obst. 1907 Sep. p. 969.

30. KIRBY. N.Y.M.J. 1907 Nov.

31. MYER. Zeit. f. Gyn. 1908 Nov.

32. GEMINDER. Beit. zur Geb. und Gynäk. XII No 2 1907

33. SINCLAIR. Lancet 1908 May p. 1541.

34. BERTINO. Ginecologia 1907 Oct. abstr. in J. Am.
Med. Ass. 1908 Jan.

35. BUIST. B.M.J. 1908 II p. 808.

36. CROOM. Tr. Edin. Obst. Soc. 1908 - 9 p. 213.
J. Obst. and Gynac. Brit. Emp. 1909
XXI p. 16 - 20.